

- (ii) expressing said DNA molecule in a suitable host cell, or expression system, together with a DNA molecule that encodes an antibody molecule light chain of the same specificity as the heavy chain, to produce an antibody molecule containing said introduced cysteine residue;
- (iii) purifying said antibody molecule from said host cell or expression system;
- (iv) contacting said purified antibody molecule with an amount of a suitable reducing agent sufficient to partially reduce the intra or inter molecular disulfide bonds of said antibody molecule and thereby enhance the formation of antibody dimers; and
- (v) contacting the purified antibody molecule with another antibody molecule having antigen specificity other than the antigen specificity of the antibody molecule purified in step (iii) and which does not have a cysteine group introduced therein; and allowing sufficient time for the dimerization reaction to proceed; thereby producing said antibody heterodimer.

24. A method for producing an antibody heterodimer composed of two different antibody molecules having binding specificity to two distinct antigens, wherein the method comprises:

- (i) obtaining or constructing a DNA molecule that encodes an antibody molecule heavy chain that has binding specificity and introducing at least one cysteine codon therein via recombinant DNA mutagenesis, wherein the location of the cysteine does not interfere with the antigen binding properties of the heterodimer;

obtaining or constructing a DNA molecule that encodes an antibody molecule light chain of the same specificity as the

heavy chain, to produce an antibody molecule containing said introduced cysteine residue:

- (iii) purifying said antibody molecule from said host cell or expression system;
- (iv) contacting said purified antibody molecule with an amount of a suitable reducing agent sufficient to partially reduce the intra or inter molecular disulfide bonds of said antibody molecule and thereby enhance the formation of antibody dimers; and
- (v) adding a thiol reactive group introduced on another antibody molecule having antigen specificity other than the antigen specificity of the antibody molecule purified in step (iii) and which does not have a cysteine group introduced therein and allowing sufficient time for the dimerization reaction to proceed; thereby producing said antibody heterodimer.

37. A method for producing an antibody heterodimer composed of two different antibody molecules having binding specificity to two distinct antigens, wherein the method comprises:

- (i) obtaining a DNA molecule that encodes an antibody molecule heavy chain that has binding specificity and introducing at least one cysteine codon via recombinant DNA mutagenesis, wherein the location of the cysteine does not interfere with the antigen binding properties of the heterodimer;
- (ii) expressing said DNA molecule in a suitable host cell, or expression system, together with a DNA molecule that encodes an antibody molecule light chain of the same specificity as the

- (iii) purifying said antibody molecule from said host cell or expression system:
- (iv) contacting said purified antibody molecule with an amount of a suitable reducing agent sufficient to partially reduce the intra or inter molecular disulfide bonds of said antibody molecule and thereby enhance the formation of antibody dimers; and cross-linking the reduced antibody molecules using a BIS-maleimido crosslinker thereby producing said antibody heterodimer.